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EXAMINER	
REDDIG, PETER J	
ART UNIT	**PAPER NUMBER**
1642	

NOTIFICATION DATE	DELIVERY MODE
09/26/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/525,672	HANISCH, FRANZ-GEORG	
	Examiner	Art Unit	
	PETER J. REDDIG	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 25-67* is/are pending in the application.

4a) Of the above claim(s) *26-30,33-50 and 59-67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,25,31,32,51-53 and 55-58* is/are rejected.

7)☒ Claim(s) *54* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/24/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Election filed April 14, 2008 in response to the Office Action of January 10, 2008 is acknowledged and has been entered.

Applicant's election with traverse of Group I, claims 1-6, 25, and 51-58 is acknowledged.

Applicant argues that the claims of Group I (claims 1-6, 25, and 51 - 58) and Group IV (claims 31 and 32) should be examined together. The claims of Group I are drawn to a product (a peptide of at least 9 amino acids in length derived from the tandem repeat domain of MUC 1 and having the amino acid sequence SAP at its N- terminus), while the claims of Group IV are drawn to a product by process (e.g., the product of claims 1-6, 25, and 51-58 made by the method recited in claim 27). The Office states:

> Inventions of Groups I, II, IV, and VII represent separate and distinct products which are made by materially different methods, and are used in materially different methods which have different modes of operation, different functions and different effects...The peptide of Group I can be produced by linking amino acids via peptide bonds and can be used for antibody synthesis .... while the peptide of Group IV is produced by providing a peptide comprising tandem repeat domain of MUC 1 or a part thereof and contacting the peptide with an effective amount of cathepsin-L and can be used for diagnostic purposes.

(Office Action, p. 4). The Office concludes that the inventions of Groups I and IV are not so linked as to form a single general inventive concept under PCT Rule 13.1, and thus, "the examination of all groups would require different searches in the U.S. Patent shoes and the scientific literature and would require the consideration of different patentability issues" (Office Action, pp. 4-5). Applicant respectfully disagrees.

Applicant argues that the claims of Groups I and IV should be examined together because the peptide products of claims 1-6, 25, 31, 32, and 51-58 share the same special technical features. The M.P.E.P. § 1850(I) states

> Unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more special technical features. The term "special technical features" is defined as meaning those technical features that define a contribution which each of the inventions considered as a whole, makes over the prior art. The determination is made based on the contents of the claims as interpreted in light of the description and drawings.

Applicant argues that in this case, the claims of Groups I and IV are directed to the same peptide product or to a molecule that includes the peptide product. The peptide products share the same minimum length requirement (at least 9 amino acids in length), are based upon the same sequences (derived from the tandem repeat domain of MUC 1), and have the same structural features (the amino acid sequence SAP at the N-terminus of the peptide). Thus, the peptide recited in the claims of Groups I and IV are not structurally and chemically different; they share the same special technical features. Accordingly, the claims of Groups I and IV should be examined together.

Applicant argues that the because the claims of Groups I and IV are directed to peptide products having the same special technical features, an examination of the subject matter of the claims of these two groups would require the same search. Furthermore, Applicant notes that the subject matter of Group IV was considered during examination of the international application (PCT/EP03/09882) to have unity with the subject matter of Group I (see, e.g., International

Search Report dated November 30, 2004). For this reason, it is believed that there would be no additional burden on the Office to search the subject matter of Groups I and IV together.

Applicant argues that the differing examples given by the Office for the uses of the peptides of Groups I and IV (i.e., a peptide for antibody synthesis and a peptide for diagnostic purposes, respectively) are not unique to the respective peptide products. In other words, the peptide of Group IV could just as readily be used to produce an antibody, while the peptide of Group I could be used for diagnostic purposes. Thus, the Office's conclusion that the peptide products of Groups I and IV represent separate and distinct products is in error and should not form the basis for restricting the inventions of Groups I and IV. The claims of Groups I and IV should be examined together

Applicants' arguments have been considered and have been found persuasive and Groups I and IV will be rejoined for examination. However, the lack of unity is maintained for the rest of the enumerated Groups for the reasons previously set forth and for these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

2. Claims 1-6 and 25-67 are pending.

3. Claims 26-30, 33-50, and 59-67 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

4. Claims 1-6, 25, 31, 32, and 51-58 are currently under consideration.

Priority

5. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Specification

6. The specification is objected for improper disclosure of amino acid sequences without a respective sequence identifier, i.e. SEQ ID NOs:, see Fig. 1, 3, 6, page 26-line9, and tables 1-4. Hence, the disclosure fails to comply with the requirements of 37 CFR 1.821 through 1.825.In the absence of a sequence identifier for each sequence, Applicant must provide a computer readable form (CRF) copy of the sequence listing, an initial or substitute paper copy of the sequence listing, as well as any amendment directing its entry into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e-f) or 1.825(b) or 1.825(d). *Failure to supply the appropriate sequences identification numbers in response to this action will be considered non-responsive.*

Claim Objections

7. Claim 1 is objected to because of the following informalities: A word, such as "at", appears to be missing between the words "of" and "least". Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 1-6 and 25 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 1-6 and 25, as written, do not sufficiently distinguish over MUC1 polypeptides as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S.

303, 206 USPQ 193 (1980). In order to obviate the instant rejection, the Examiner suggests that the claims should be amended to indicate the hand of the inventor, e.g., by insertion of "isolated" or "purified" provided the support for such an amendment can be identified in the specification as originally filed. See MPEP 2105.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 31, 32, 51-53 and 55-58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a peptide comprising SEQ ID NO: 1 or 11 and compositions comprising SEQ ID NO: 1 or 11 and a pharmaceutically acceptable carrier, *does not* reasonably provide enablement for a peptide of least 9 amino acids in length derived from the tandem repeat domain of MUC1 and having the amino acid sequence SAP at its N-terminus, SEQ ID NOs:2-4, variants of SEQ ID NOs:1-4, and 11, a peptide obtainable by the method of claim 27, a composition comprising a therapeutically effective amount of a peptide or fusion molecule comprising at least 9 amino acids of the tandem repeat domain of MUC1 add having the amino acid sequence SAP at its N-terminus or an antigen presenting cell comprising said peptide or fusion molecule and a pharmaceutically acceptable carrier, or a composition comprising a therapeutically effective amount of a peptide or fusion molecule comprising at least 9 amino acids of the tandem repeat domain of MUC1 add having the amino acid sequence SAP at its N-terminus or an antigen presenting cell comprising said peptide or fusion molecule and a pharmaceutically acceptable carrier, which is a vaccine. The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are broadly drawn to a peptide of least 9 amino acids in length derived from the tandem repeat domain of MUC1 and having the amino acid sequence SAP at its N-terminus, SEQ ID NOs:1-4, and 11, variants of SEQ ID NOs:1-4, and 11, and compositions and vaccines comprising said peptides.

Given their broadest reasonable interpretation, the claims are drawn to a very large genus of peptides with the only common structural requirement being the amino acid sequence SAP at its N-terminus and antigen presenting cells comprising said peptides. It is noted that given that the specification teaches that the amino acid SAP does not need to be immediately at the N-terminus, but may be preceded by one or more amino acids, see p.8– lines 15-17, the claims encompass peptides in which SAP is located anywhere within the peptide, except for at the immediate C-terminus.

The specification teaches that the present invention relates to MUCl peptides and to methods of producing those peptides. The invention further relates to an ex vivo-method of producing a population of autologous antigen presenting cells which are capable of inducing effective immune responses against MUC1. The specification teaches that the invention also relates to APCs, which are obtainable by these methods as well as to the use of the above mentioned peptides and APCs in a pharmaceutical composition for the treatment of breast cancer or other MUC1-positive carcinomas including colorectal, pancreatic and gastric carcinomas, see p. 1-lines 5-11. The specification teaches that the peptides, fusion molecules and APCs, and compositions containing any one of those compounds can be used as vaccine, for example for the prevention and therapeutic treatment of MUC1-positive carcinomas such as breast, colorectal, pancreatic and gastric cancer, see p. 4- lines 7-10.

Given the above it is assumed for examination purposes that the intended use of the claimed peptides is for the prevention and therapeutic treatment of MUC1-positive carcinomas such as breast, colorectal, pancreatic and gastric cancer by using the peptides as an immunogenic vaccine.

The specification teaches that, while there is a constant need of specific and immunogenic MUCl peptides for use as anti-cancer vaccines, so far the structural requirements for designing immunogenic MUCl peptides had not been elucidated see p. 2-line 26-28.

The specification teaches that SEQ ID NO: 11/SAP17 is produced by dendritic cells pulsed with MUC1 peptides through a cathepsin L dependent process, see p. 7, lines 1-19. Moreover, the specification teaches that SEQ ID NO: 11/SAP17 peptides and their glycosylated derivatives may represent a "preprocessed" form suitable for external loading on MHC class II

molecules in irnmunotherapeutic approaches. In loading experiments with SAP17 the glycosylation-dependent effects on the binding to MHC class 11 proteins and on recognition by the T cell receptors can now be studied by systematic variation of the substitution sites and structures of the glycans, see p. 37. .

One cannot extrapolate the teaching of the specification to the scope of the claims because the claims as written are drawn to a large genus of peptides derived from the tandem repeat of MUC1 and neither the specification nor the art of record define which amino acid residues are critical to the induction of an immune response against MUC1 so the that peptides will either tstimulate antibodies that are specific for MUC1 or which will be able to stimulate T cells by direct administration or through antigen presenting cells comprising the peptide that recognize MUC1 positive tumor cells. As drawn to antibodies, Bowie et al (Science, 1990, 257:1306-1310), teaches that an amino acid sequence encodes a message that determines the shape of a protein and determines the ability of said protein to fold into unique three-dimensional structures that allows them to function. Bowie further teaches that certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (p. 1306, cols 1 and 2). Clearly, the three dimension structure of a protein is critical to the production of antibodies given the teaching of Herbert et al (The Dictionary of Immunology, Academic Press, 3rd Edition, London, 1985, pages 58-59). Herbert et al who specifically teach that an epitope is the region on an antigen molecule to which antibody specifically binds. B cell epitopes on protein antigens are of variable size comprising up to about 20 amino acids. Antibodies bind in a more or less exact three dimensional fit with an epitope. This may be formed from residues on different regions of

a protein antigen molecule which, in the native state, are closely apposed due to protein folding. Thus the three-dimensional structure of the protein molecule may be essential for antibody binding. (p. 58). However, neither the specification nor the art of record provide teachings that provide information about the residues critical for epitopes required for the establishment of an immune response that will produce antibodies that recognize full-length MUC1. This information appears to be critical because the art recognizes (see Bowie above) that it is the protein sequence that determines the three dimensional shape of a protein and Herbert et al specifically state that antibodies bind in a more or less exact three dimensional fit and suggests that the three-dimensional structure of the protein molecule may be essential for antibody binding. Thus, in the absence of guidance in the specification, the effects of the undefined derivatives of the MUC1 and variants of SEQ ID NOs: 1-4 and 11 on the three-dimensional structure of the claimed isolated protein cannot be predicted by one of skill in the art and the ability of antibodies generated by such variants to bind MUC1 cannot be predicted by one of skill in the art with a reasonable expectation of success. Further, the sensitivity of protein binding interactions to alterations of even a single amino acid in a sequence are exemplified by Abaza et al. (Journal of Protein Chemistry, Vol. 11, No. 5, 1992, pages 433-444, see abstract in particular) who teach single amino acid substitutions outside the antigenic site on a protein affects antibody binding. Further, the sensitivity of binding proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess et al (J of Cell Bio. 111:2129-2138, 1990) who teach that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. These references demonstrate that even a single amino

acid alteration or what appears to be an inconsequential chemical modification will often dramatically affect the characteristics of protein binding interactions. Thus it would not be expected that antibodies generated against one of the peptide derivatives and variants of the tandem repeat domain of MUC1 would predictably recognize MUC1 bearing tumor cells and thus, would not be effect for treatment or prevention of cancers that express MUC1. Given the above undue experimentation would be required make and use the broadly claimed invention.

Further, as drawn to recognition of MUC1 by T-cells from patients cancer, Herbert et al, *Supra*, teaches that T-cells recognize peptide fragments which have been processed by an accessory cell and presented in the cleft of a class I MHC antigen or a class II MHC antigen and that a continuous primary sequence is necessary for T cell recognition (p. 58). It is obvious that T cell epitopes and antibody epitopes are not the same. However, the issues drawn to the lack of guidance in the specification as to critical residues and polypeptide fragments required for T cell binding are relevant to the broadly claim genus of peptides as well. In particular, George et al. (2005, Trends in Immunology 26(12):653-659) teach that the specificity of the interaction with which a T-cell receptor recognizes antigen in the form of a peptide held in the groove of an MHC class molecule is such that a single amino acid substitution in the peptide can abolish the ability of T cells to respond to the antigen or can convert the peptide to an antagonist peptide that "turns off" the ability of a population of T cells to respond by proliferation. Given that the sequences critical for T-cell recognition of this broadly claimed genus of peptides have not been defined by the specification, it could not be predicted which of these peptides would effectively stimulate a T-cell response, nor could it be predicted which of these broadly claimed peptides, even if they

comprised a T-cell epitope, would stimulate a T-cell response directed against a MUC-1 expressing cancer cell, without undue experimentation.

Furthermore, peptide based tumor immunotherapy either through direct administration or via peptide pulsed antigen presenting cells is well known in the art to be unpredictable. In particular, Celis (J of Clinical Investigation, 2002, 110:1765-1768) summarize the problems associated with peptide vaccine failure. Celis teaches that the advantages that peptide vaccines have to offer are diminished by their inherent lack of immunogenicity which so far has been reflected by their not-so-spectacular results in the clinic. Vaccines consisting of peptides are likely to be ignored and will likely be ineffective at inducing T-cell immunity. Peptides that are injected in aqueous solutions will be unsuccessful at stimulating CTL responses, either because of rapid biodegradation (e.g., by proteases) or, worse, because of the induction of T-cell tolerance/anergy, which results from the antigenic stimulation of CTLs by nonprofessional APCs. An additional complication resulting from the use of synthetic peptide-derived vaccines is the induction of CTLs that, while capable of killing target cells that are exogenously pulsed with peptide, are not able to recognize target cells that naturally process and present the peptide epitope, such as infected or malignant cells. Obviously, these "low-quality" CTLs would have little effect in fighting and controlling disease. One reason for generation of such low-quality CTLs by peptide vaccine is the induction of CTLs with low affinity for antigen, which will require a high density of specific peptide/MHC complexes on the target-cell surface to exert their effector function. *In vitro*, the induction of low-affinity CTLs usually results from the use of high concentrations of peptide, generating a high level of specific peptide/MHC complexes on APCs, which will effectively activate these CTLs. The prediction is that high densities of peptide/MHC

complexes on APCs *in vivo* resulting from an excessive peptide dose will also produce low-quality CTLs with low affinity for the antigen. Finally, another cause for the induction of low-quality CTLs is the use of vaccines produced with synthetic peptides representing cryptic T cell epitopes, which are not expressed on the surface of the infected or tumor target cells. CTLs recognizing cryptic epitopes will be unable to interact with infected or tumor target cells and will also be useless in disease control (p. 1765).

Additionally, as the treatment or prevention of cancer as contemplated in the specification, appears to be dependent in part on a T-cell mediated anti-tumor response, it is well known in the art that tumor therapies dependent on T-cell immune responses are unpredictable. In particular Marincola et al. (Trends in Immunology, June 2003, 334-341) teach "…most human tumors do not regress and continue to grow in spite of spontaneous or immunization-induced immune responses demonstrated in circulating lymphocytes. Indeed, systemic immune responses might insufficiently address the complexity of tumor–host interactions because of factors, such as (1) the lack of productive T-cell receptor (TCR) engagement with epitope owing to qualitative and/or quantitative defects in the generation and maintenance of the immune response, (2) insufficient co-stimulation provided by the host, (3) the lack of localization of the immune response in target tissues and (4) the complexity of tumor–host interactions within the tumor microenvironment caused by temporal changes in tumor phenotypes and an array of immune mediators expressed in the tumor microenvironment", see Abstract. Additionally, Kirkin et al (1998, APMIS, 106: 665-679) teach that for some antigens, in particular for tumor antigens, due to the existence of self-tolerance, only T cells with low affinity T-cell receptors are produced (abstract). Additionally, Sherman et al, (Critical Reviews in Immunol. 1998, 18:47-54) teach that

self-tolerance may eliminate T cells that are capable of recognizing T-cell epitopes with high avidity. Smith (Clin. Immunol, 1994, 41(4): 841-849), teaches that antigen overload, due to antigen shedding by actively growing tumor, could block specifically either cytotoxic or proliferative responses of tumor specific T cells (p. 847, last paragraph bridging p.848 and p.848). Smith further teaches that many tumors progressively lose MHC representation at the surface of the cell, and the loss of surface Class I MHC could severely limit the possibilities for cytotoxic T cells specific for a tumor specific antigen to find said tumor specific antigen in the necessary MHC context (p.484). Furthermore, Harlin et al. (Caner Immunol. Immunotherap. 2006, 55:1185-1197) teach that although melanoma tumors usually express antigens that can be recognized by T cells, immune-mediated tumor rejection is rare, see Abstract. Additionally, Harlin et al. teach that in a melanoma patient with a CD8+ T cells that recognize Melan-A, despite the recruitment of large numbers of activated CD8+ T cells into the tumor microenvironment, T cell hyproresponsiveness and additional negative regulatory mechanism can limit the effector phase of the anti-tumor immune response, see Abstract.

Although the level of skill in the art is high, given the unpredictability in the art of stimulating T-cells for cancer immunotherapy, given the unpredictability of generating MUC-1 specific immune response, antibody or t-cell mediated, with the broadly claimed genus of peptides, in the absence of sufficient guidance or exemplification in the specification for the broadly claimed genus peptides that would provide one of skill in the art direction to make and use the peptides as contemplated and claimed, undue experimentation would be required for one of skill in the art to use the broadly claimed invention. It is also noted that SEQ ID NO: 2-4 are not completely homologous to the MUC1 protein, and given that neither the specification nor the

art of record has demonstrated that these peptides could be used as contemplated, undue experimentation would be required to use them for the prevention or treatment of cancer as contemplated.

Additionally, as drawn to using the peptides as a vaccine the specification teaches that a vaccine is for the prevention and therapeutic treatment of MUC1-positive carcinomas such as breast, colorectal, pancreatic and gastric cancer, see p. 4- lines 7-10. Given that the specification teaches that vaccines are, in part, for the prevention of cancer and it is well known in the art that vaccines are used for prevention, one of skill in the art cannot extrapolate the teaching of the specification to the enablement of the claims because the specification does not provide examples or guidance for the prevention of cancer comprising administering to a subject a therapeutically effective amount of the claimed peptides. The specification lacks the critical steps necessary in presenting some type of predictable response in a population of hosts deemed necessary to prevent cancer. Reasonable guidance with respect to preventing any cancer relies on quantitative analysis from defined populations which have been successfully pre-screened and are predisposed to particular types of cancer or have had cancer. The essential element towards the validation of a preventive therapeutic is the ability to test the drug on subjects monitored in advance of clinical cancer and link those results with subsequent histological confirmation of the presence or absence of disease. This irrefutable link between antecedent drug and subsequent knowledge of the prevention of the disease is the essence of a valid preventive agent. Further, a preventive administration also must assume that the therapeutic will be safe and tolerable for anyone susceptible to the disease. All of this underscores the criticality of providing workable examples which are not disclosed in the specification

With regards to the prevention of cancer in a mammal comprising administering the claimed peptides, the specification does not disclose sufficient guidance or objective evidence that such peptides would predictably prevent the formation of cancer cells in a mammal. The prevention of cancer, let alone the prevention of cancer with peptides, is highly unpredictable. The majority of studies suggest that the essential element towards the validation of a preventive therapeutic is the ability to test the drug on subjects monitored in *advance* of clinical cancer and *link* those results with subsequent histological confirmation of the presence or absence of disease. Further, such studies require the appropriate experimental models for analyzing chemo- or immunoprevention. For example, Byers, T. (CA Journal, Vol. 49, No. 6, Nov/Dec. 1999) teaches that randomized controlled trials are commonly regarded as the definitive study for proving causality (1st col., p.358), and that in controlled trials the random assignment of subjects to the intervention eliminates the problems of dietary recalls and controls the effects of both known and unknown confounding factors. Further, Byers suggests that chemo-preventative trials be designed "long-term" such that testing occurs over many years (2nd col., p. 359). The specification is devoid of any models or experimental analysis that reasonably suggests that the claimed peptides would predictably prevent the formation of cancer. This, combined with the state of the art of preventing cancer, although the skill in the art is high, suggests that undue experimentation would be required to practice the invention as broadly claimed.

The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the invention will function as contemplated or claimed with a reasonable expectation of success. For the above

reasons, it appears that undue experimentation would be required to practice the claimed invention.

9. Claims 1-5, 31, 32, 51-53, 55, 56 and 58 are rejected as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a peptide of least 9 amino acids in length derived from the tandem repeat domain of MUC1 and having the amino acid sequence SAP at its N-terminus, SEQ ID NOs:1-4, and 11, variants of SEQ ID NOs:1-4, and 11, and compositions and vaccines comprising said peptides. When given the broadest reasonable interpretation, the claims are drawn to a very large genus of peptides with the only common structural requirement being the amino acids SAP at its N-terminus and antigen presenting cells produced with said peptides. It is noted that given that the specification teaches that the amino acid SAP does not need to be immediately at the N-terminus, but may be preceded by one or more amino acids, see p.8– lines 15-17, the claims encompass peptides in which SAP is located anywhere within the peptide, except for at the immediate C-terminus. Thus the genus of peptides is highly variant that vary significantly both in structure and function from each other. The description of SEQ ID NOs: 1-4 and 11 fails to adequately describe the genus of peptides because said genus tolerates members which differ significantly in both structure and function from SEQ ID NOs: 1-4 and 11. One of skill in the art can reasonably conclude that applicant was not in possession of a genus of peptide of least 9 amino acids in length derived from the tandem repeat domain of MUC1 and having the amino acid sequence SAP at its N-terminus, SEQ ID NOs: 1-4, and 11,

variants of SEQ ID NOs: 1-4, and 11, and compositions and vaccines comprising said peptides at the time the invention was filed.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

It is noted that as of the filing date a few peptides of least 9 amino acids in length derived from the tandem repeat domain of MUC1 and having the amino acid sequence SAP at its N-terminus, were known in the art (see for example, U.S. 5,989,552, 6,177,256, and 5,827,666), however, these few peptides fails to adequately describe an entire genus because the genus is highly variant encompassing members which differ significantly in structure from the art known peptides.

In the instant case the genus is only described as a definition by function (i.e. treatment or prevention of cancer), and beyond that of a few examples of peptides known in the art, one of skill in the art cannot readily visualize or recognize the identity of members of the broadly claimed genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1, 2, 3, 4, 31, 32, 51-53 and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent No. 5,989,552 (McKenzie et al. Nov. 23, 1999) as evidenced by Appendix 1.

US Patent No. 5,989,552 teaches SEQ ID NO: 1 from the tandem repeat of MUC1, which comprises SEQ ID NO: 1 and 11 of the instant application, see Appendix 1 and col. 1. US Patent No. 5,989,552 teaches making fusion proteins with the MUC-1 peptides of the invention,

see col. 3-lines 49-67. US Patent No. 5,989,552 teaches using the MUC-1 peptides of the invention in vaccines in pharmaceutically acceptable carriers, see col. 5-lines 36-64.

In regard to claims 31 and 32 the prior art peptide functions in the same manner as the claimed peptide and the patentability of a product-by-process claim is determined by the novelty and nonobviousness of the claimed product itself without consideration of the process for making it which is recited in the claim. In re Thorpe, 227 USPQ 964 (Fed. Cir. 1985).

11. Claims 1, 2, 3, 4, 31, 32, 51-53 and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent No. 6,177,256 (McKenzie et al. January 23, 2001) as evidenced by Appendix 2.

US Patent No. 6,177,256 teaches SEQ ID NO: 1, which comprises SEQ ID NO: 1 and 11 of the instant application, see Appendix 2 and col. 1. US Patent No. 6,177,256 teaches making fusion proteins with the MUC-1 peptides of the invention, see col. 3-lines 49-67. US Patent No. 6,177,256 teaches using the MUC-1 peptides of the invention in vaccines in pharmaceutically acceptable carriers, see col. 5-lines 36-64.

In regard to claims 31 and 32 the prior art peptide functions in the same manner as the claimed peptide and the patentability of a product-by-process claim is determined by the novelty and nonobviousness of the claimed product itself without consideration of the process for making it which is recited in the claim. In re Thorpe, 227 USPQ 964 (Fed. Cir. 1985).

12. Claims 1, 2, 3, 4, 31, 32, 51-53 and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent No. 5,827,666 (Finn et al. October 27, 1998) as evidenced by Appendix 3.

US Patent No. 5,827,666 teaches SEQ ID NO: 28, which comprises SEQ ID NO: 1 and 11 of the instant application, see Appendix 3. US Patent No. 5,827,666 teaches making fusion proteins with the MUC-1 peptides of the invention, see col. 5-lines 30-43. US Patent No. 5,827,666 teaches using the MUC-1 peptides of the invention in vaccines in pharmaceutically acceptable carriers, see col. 6-lines 5-20 and col. 10-lines 22-30.

In regard to claims 31 and 32 the prior art peptide functions in the same manner as the claimed peptide and the patentability of a product-by-process claim is determined by the novelty and nonobviousness of the claimed product itself without consideration of the process for making it which is recited in the claim. In re Thorpe, 227 USPQ 964 (Fed. Cir. 1985).

13. Claims 1-6, 31, 32, 51-53 and 55-58 are rejected under 35 U.S.C. 102(b) as being anticipated by Nishimori et al. (J. Biol. Chem. June 10, 1994 269:16123-16130).

Nishimori et al. teach a peptide that comprises SEQ ID NO: 1 and is O-glycosylated at Thr 5 and 12 of SEQ ID NO: 1, see the Abstract, Fig. 3 and page 16,126. Nishimori et al. teach eluting the peptides after purification into the pharmaceutically acceptable carrier water, see p. 16,124- 1st col.

It is noted that given that the specification teaches that the amino acid SAP does not need to be immediately at the N-terminus, but may be preceded by one or more amino acids, see p.8– lines 15-17, the claims encompass peptides in which SAP is located anywhere within the peptide, except for at the immediate C-terminus.

In regard to claims 31 and 32 the prior art peptide functions in the same manner as the claimed peptide and the patentability of a product-by-process claim is determined by the novelty

and nonobviousness of the claimed product itself without consideration of the process for making it which is recited in the claim. In re Thorpe, 227 USPQ 964 (Fed. Cir. 1985).

It is noted that the intended uses of the claimed peptides as a vaccine is not given weight for comparison of the claims with the prior art because a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art.

14. Claims 1, 2, 3, 4, 31, 32, 51-53 and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Japanese Patent No. JP 7051065 (February 1995) as evidenced by Appendix 4 and its translation (Exhibit 1).

Japanese Patent No. JP 7051065 teaches glycoprotein 39 which comprises SEQ ID NO: 2 of the instant Application, see Appendix 4.

One of skill in the art would immediately envision putting the peptide in a pharmaceutically acceptable carrier, such Phosphate buffered saline, for storage and use.

It is noted that given that the specification teaches that the amino acid SAP does not need to be immediately at the N-terminus, but may be preceded by one or more amino acids, see p.8– lines 15-17, the claims encompass peptides in which SAP is located anywhere within the peptide, except for at the immediate C-terminus.

In regard to claims 31 and 32 the prior art peptide functions in the same manner as the claimed peptide and the patentability of a product-by-process claim is determined by the novelty and nonobviousness of the claimed product itself without consideration of the process for making it which is recited in the claim. In re Thorpe, 227 USPQ 964 (Fed. Cir. 1985).

It is noted that the intended uses of the claimed peptides as a vaccine is not given weight for comparison of the claims with the prior art because a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art.

15. Claim 54 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

16. No claims allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to PETER J. REDDIG whose telephone number is (571)272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Helms Larry can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Peter J Reddig/
Examiner, Art Unit 1642
/P. J. R./

/Karen A Canella/
Primary Examiner, Art Unit 1643

Appendix 1

```
SEQ ID NO:  1 Alignment
US-08-833-807-1
; Sequence 1, Application US/08833807
; Patent No. 5989552
;  GENERAL INFORMATION:
;    APPLICANT:  McKenzie, Ian F.C.
;    APPLICANT:  Apostolopoulos, Vasso
;    APPLICANT:  Pietersz, Geoff A.
;    TITLE OF INVENTION:  ANTIGENIC CARBOHYDRATE COMPOUNDS AND
;    TITLE OF INVENTION:  THEIR USE IN IMMUNOTHERAPY
;    NUMBER OF SEQUENCES:  14
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Dann Dorfman Herrell and Skillman
;      STREET:  Suite 720, 1601 Market Street
;      CITY:  Philadelphia
;      STATE:  Pennsylvania
;      COUNTRY:  United States of America
;      ZIP:  19103-2307
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.30
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/833,807
;      FILING DATE:
;      CLASSIFICATION:  424
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  US 08/340,711
;      FILING DATE:  16-NOV-1994
;      APPLICATION NUMBER:  AU PM3223
;      FILING DATE:  24-DEC-1993
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Hagan, Patrick J.
;      REGISTRATION NUMBER:  27,643
;      REFERENCE/DOCKET NUMBER:  530547/PAS/MKR
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (215)563-4100
;      TELEFAX:  (215)563-4044
;  INFORMATION FOR SEQ ID NO:  1:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  20 amino acids
;      TYPE:  amino acid
;      STRANDEDNESS:
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  peptide
US-08-833-807-1

  Query Match             100.0%;  Score 109;  DB 1;  Length 20;
  Best Local Similarity   100.0%;  Pred. No. 2.8e-07;
  Matches   20;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 SAPDTRPAPGSTAPPAHGVT 20
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Db          1 SAPDTRPAPGSTAPPAHGVT 20


SEQ ID NO:  11 Alignment

US-08-833-807-1
; Sequence 1, Application US/08833807
; Patent No. 5989552
;  GENERAL INFORMATION:
;    APPLICANT:  McKenzie, Ian F.C.
;    APPLICANT:  Apostolopoulos, Vasso
;    APPLICANT:  Pietersz, Geoff A.
;    TITLE OF INVENTION:  ANTIGENIC CARBOHYDRATE COMPOUNDS AND
;    TITLE OF INVENTION:  THEIR USE IN IMMUNOTHERAPY
;    NUMBER OF SEQUENCES:  14
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Dann Dorfman Herrell and Skillman
;      STREET:  Suite 720, 1601 Market Street
;      CITY:  Philadelphia
;      STATE:  Pennsylvania
;      COUNTRY:  United States of America
;      ZIP:  19103-2307
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.30
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/833,807
;      FILING DATE:
;      CLASSIFICATION:  424
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  US 08/340,711
;      FILING DATE:  16-NOV-1994
;      APPLICATION NUMBER:  AU PM3223
;      FILING DATE:  24-DEC-1993
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Hagan, Patrick J.
;      REGISTRATION NUMBER:  27,643
;      REFERENCE/DOCKET NUMBER:  530547/PAS/MKR
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (215)563-4100
;      TELEFAX:  (215)563-4044
;  INFORMATION FOR SEQ ID NO:  1:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  20 amino acids
;      TYPE:  amino acid
;      STRANDEDNESS:
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  peptide
US-08-833-807-1

  Query Match             100.0%;  Score 94;  DB 1;  Length 20;
  Best Local Similarity   100.0%;  Pred. No. 1.3e-05;
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Qy          1 SAPDTRPAPGSTAPPAH 17
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Db          1 SAPDTRPAPGSTAPPAH 17
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Appendix 2

SEQ ID NO: 1 alignment

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; Sequence 1, Application US/09223043
; Patent No. 6177256
;  GENERAL INFORMATION:
;    APPLICANT:  McKenzie, Ian F.C.
;    APPLICANT:  Apostolopoulos, Vasso
;    APPLICANT:  Pietersz, Geoff A.
;    TITLE OF INVENTION:  ANTIGENIC CARBOHYDRATE COMPOUNDS AND
;    TITLE OF INVENTION:  THEIR USE IN IMMUNOTHERAPY
;    NUMBER OF SEQUENCES:  14
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Dann Dorfman Herrell and Skillman
;      STREET:  Suite 720, 1601 Market Street
;      CITY:  Philadelphia
;      STATE:  Pennsylvania
;      COUNTRY:  United States of America
;      ZIP:  19103-2307
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.30
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/09/223,043
;      FILING DATE:
;      CLASSIFICATION:
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  08/833,807
;      FILING DATE:
;      APPLICATION NUMBER:  AU PM3223
;      FILING DATE:  24-DEC-1993
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Hagan, Patrick J.
;      REGISTRATION NUMBER:  27,643
;      REFERENCE/DOCKET NUMBER:  530547/PAS/MKR
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (215)563-4100
;      TELEFAX:  (215)563-4044
;  INFORMATION FOR SEQ ID NO:  1:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  20 amino acids
;      TYPE:  amino acid
;      STRANDEDNESS:
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  peptide
US-09-223-043-1

  Query Match             100.0%;  Score 109;  DB 2;  Length 20;
  Best Local Similarity   100.0%;  Pred. No. 2.8e-07;
  Matches   20;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 SAPDTRPAPGSTAPPAHGVT 20
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              ||||||||||||||||||||
Db          1 SAPDTRPAPGSTAPPAHGVT 20

SEQ ID NO:  11 alginment
US-09-223-043-1
; Sequence 1, Application US/09223043
; Patent No. 6177256
;  GENERAL INFORMATION:
;    APPLICANT:  McKenzie, Ian F.C.
;    APPLICANT:  Apostolopoulos, Vasso
;    APPLICANT:  Pietersz, Geoff A.
;    TITLE OF INVENTION:  ANTIGENIC CARBOHYDRATE COMPOUNDS AND
;    TITLE OF INVENTION:  THEIR USE IN IMMUNOTHERAPY
;    NUMBER OF SEQUENCES:  14
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Dann Dorfman Herrell and Skillman
;      STREET:  Suite 720, 1601 Market Street
;      CITY:  Philadelphia
;      STATE:  Pennsylvania
;      COUNTRY:  United States of America
;      ZIP:  19103-2307
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.30
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/09/223,043
;      FILING DATE:
;      CLASSIFICATION:
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  08/833,807
;      FILING DATE:
;      APPLICATION NUMBER:  AU PM3223
;      FILING DATE:  24-DEC-1993
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Hagan, Patrick J.
;      REGISTRATION NUMBER:  27,643
;      REFERENCE/DOCKET NUMBER:  530547/PAS/MKR
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (215)563-4100
;      TELEFAX:  (215)563-4044
;  INFORMATION FOR SEQ ID NO:  1:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  20 amino acids
;      TYPE:  amino acid
;      STRANDEDNESS:
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  peptide
US-09-223-043-1

  Query Match             100.0%;  Score 94;  DB 2;  Length 20;
  Best Local Similarity   100.0%;  Pred. No. 1.3e-05;
  Matches   17;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 SAPDTRPAPGSTAPPAH 17
              |||||||||||||||||
Db          1 SAPDTRPAPGSTAPPAH 17
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Appendix 3

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SEQ ID NO:  1 alignment
US-08-288-059-28
; Sequence 28, Application US/08288059
; Patent No. 5827666
;  GENERAL INFORMATION:
;    APPLICANT:  FINN, OLIVERA J.
;    APPLICANT:  FONTENOT, J. D.
;    APPLICANT:  MONTELARO, RONALD C.
;    TITLE OF INVENTION:  SYNTHETIC MULTIPLE TANDEM REPEAT MUCIN
;    TITLE OF INVENTION:  AND MUCIN-LIKE PEPTIDES, AND USES THEREOF
;    NUMBER OF SEQUENCES:  36
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  CUSHMAN DARBY & CUSHMAN, L.L.P.
;      STREET:  1100 NEW YORK AVENUE, N.W.
;      CITY:  WASHINGTON
;      STATE:  D.C.
;      COUNTRY:  USA
;      ZIP:  20005
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/288,059
;      FILING DATE:  08-AUG-1994
;      CLASSIFICATION:  424
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  CHAPIN, MARLANA K.
;      REGISTRATION NUMBER:  35,843
;      REFERENCE/DOCKET NUMBER:  61137/205204
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  202-861-3711
;      TELEFAX:  202-822-0944
;      TELEX:  6714627 CUSH
;  INFORMATION FOR SEQ ID NO:  28:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  25 amino acids
;      TYPE:  amino acid
;      STRANDEDNESS:  single
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  peptide
US-08-288-059-28

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  Best Local Similarity   100.0%;  Pred. No. 3.6e-07;
  Matches   20;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

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Db          4 SAPDTRPAPGSTAPPAHGVT 23

SEQ ID NO:  11 alignment
; Sequence 28, Application US/08288059
; Patent No. 5827666
;  GENERAL INFORMATION:
;    APPLICANT:  FINN, OLIVERA J.
;    APPLICANT:  FONTENOT, J. D.
;    APPLICANT:  MONTELARO, RONALD C.
```

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;    TITLE OF INVENTION:  SYNTHETIC MULTIPLE TANDEM REPEAT MUCIN
;    TITLE OF INVENTION:  AND MUCIN-LIKE PEPTIDES, AND USES THEREOF
;    NUMBER OF SEQUENCES:  36
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  CUSHMAN DARBY & CUSHMAN, L.L.P.
;      STREET:  1100 NEW YORK AVENUE, N.W.
;      CITY:  WASHINGTON
;      STATE:  D.C.
;      COUNTRY:  USA
;      ZIP:  20005
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/288,059
;      FILING DATE:  08-AUG-1994
;      CLASSIFICATION:  424
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  CHAPIN, MARLANA K.
;      REGISTRATION NUMBER:  35,843
;      REFERENCE/DOCKET NUMBER:  61137/205204
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  202-861-3711
;      TELEFAX:  202-822-0944
;      TELEX:  6714627 CUSH
;  INFORMATION FOR SEQ ID NO:  28:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  25 amino acids
;      TYPE:  amino acid
;      STRANDEDNESS:  single
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  peptide
US-08-288-059-28

  Query Match             100.0%;  Score 94;  DB 1;  Length 25;
  Best Local Similarity   100.0%;  Pred. No. 1.7e-05;
  Matches   17;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 SAPDTRPAPGSTAPPAH 17
              |||||||||||||||||
Db          4 SAPDTRPAPGSTAPPAH 20
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Appendix 4

```
AAR96297
ID   AAR96297 standard; peptide; 60 AA.
XX
AC   AAR96297;
XX
DT   26-JUL-1996  (first entry)
XX
DE   Glycoprotein 39 N terminal fragment.
XX
KW   Glycoprotein 39; gp39; lambda gt11 cDNA library; gastric cancer;
KW   cell line KATO-III; tumour; immune abnormality; marker;
KW   inflammatory disease.
XX
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```
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1. .20
FT                   /note= "Repeat unit"
XX
PN   JP07051065-A.
XX
PD   28-FEB-1995.
XX
PF   21-FEB-1992;   92JP-00035085.
XX
PR   21-FEB-1992;   92JP-00035085.
XX
PA   (NIKO-) NIPPON KOTAI KENKYUSHO KK.
PA   (UYKA-) UNIV KAGOSHIMA.
XX
DR   WPI; 1995-127356/17.
DR   N-PSDB; AAT29189.
XX
PT   Glyco:protein 39 gene - used in the mass production of glyco:protein 39,
PT   for use as tumour and immune abnormality marker.
XX
PS   Claim 2; Page 8; 10pp; Japanese.
XX
CC   The sequences given in AAR96297-98 represent portions of glycoprotein 39.
CC   This sequence represents the N terminal portion of the glycoprotein 39
CC   gene. The cDNA encoding this sequence was isolated from lambda gt11 cDNA
CC   library derived from the gastric cancer cell line KATO-III. Glycoprotein
CC   39 is expected to be used as a tumour marker, an immune abnormality
CC   marker or a marker for various inflammatory diseases
XX
SQ   Sequence 60 AA;

  Query Match             100.0%;  Score 104;  DB 2;  Length 60;
  Best Local Similarity   100.0%;  Pred. No. 3.6e-06;
  Matches   20;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 SAPESRPAPGSTAPAAHGVT 20
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Db         12 SAPESRPAPGSTAPAAHGVT 31
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